EuroIntervention

# Quantification of stenosis severity on multidetector row computed tomography

**Mark J. Boogers[1,2], MD; Joanne D. Schuijf[1]*, PhD**

*1. Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands; 2. The Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands*

*Mark J. Boogers is supported by the Dutch Heart Foundation, grant 2006T102. J. Schuijf has no conflict of interest to declare.*

**KEYWORDS**

*Computed tomography, coronary plaques, stenosis severity, quantification*

## Abstract

A comprehensive evaluation of coronary anatomy and atherosclerosis can be provided by MDCT. Currently, several studies have used either manual or semi-automated algorithms for quantification of different plaque characteristics, in particular the degree of luminal narrowing. Although the feasibility of these quantitative algorithms has been demonstrated, further refinement of quantitative CT algorithms is currently indicated to allow a comprehensive yet fully automated analysis of plaque characteristics.

* Corresponding author: Dept Cardiology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands, Postal zone: 2300 RC
E-mail: j.d.schuijf@lumc.nl

## Introduction

Multidetector row computed tomography (MDCT) allows non-invasive evaluation of coronary artery disease (CAD) with excellent image quality and diagnostic accuracy as compared to invasive coronary angiography.[1-3] In recent years, rapid technological advances have led to an enormous increase in the use of MDCT imaging for non-invasive evaluation of patients with known or suspected coronary atherosclerosis.

One of the advantages of MDCT imaging is the fact that it provides a detailed overview of coronary anatomy (including the location of coronary ostia, coronary tree dominancy, tortuosity and coronary angulation) as well as comprehensive analysis of coronary stenosis (extent, distribution and location). Moreover, the technique is not restricted to luminography and additional important information on coronary plaques can be easily derived, including plaque morphology, degree of plaque remodelling, plaque burden and the longitudinal length of atherosclerotic lesions. Such an integrated analysis of coronary atherosclerotic disease may provide important information to risk stratify patients for potential forthcoming cardiovascular events, and while it can also be used to guide future therapeutic clinical interventions, including percutaneous coronary intervention.

At present, MDCT images are most commonly post-processed and evaluated by an experienced reader using a visual approach. However, the introduction of dedicated algorithms for automated quantification of plaque characteristics may further improve diagnostic accuracy and reproducibility of MDCT imaging. Moreover, automated quantitative approaches may reduce the amount of time required to evaluate MDCT images. Accordingly, the development and validation of novel quantitative approaches for MDCT imaging are increasingly attracting interest.

The current review will provide an overview of the currently available approaches on MDCT to quantify plaque characteristics, with particular focus on the quantification of stenosis severity. Additionally, the review will discuss the potential role of quantitative MDCT analyses to guide percutaneous coronary intervention procedures.

## Quantification of coronary artery stenosis

Invasive coronary angiography is considered the golden standard for evaluation of stenosis severity in clinical cardiology.[4] As compared to the standard of reference, MDCT imaging has been shown in several studies, including large multicentre trials, to be an accurate technique for detection of significant coronary artery luminal narrowing (≥50% stenosis).[1-3] However, despite these promising results, one of the major drawbacks of MDCT imaging remains the fact that the degree of coronary stenosis is most often determined visually using a dichotomous scoring system with 50% lumen diameter stenosis as a cutoff.[3,5] This binary approach restricts the amount of potential useful information that can be derived from MDCT imaging with regard to stenosis severity. For clinical purposes, an accurate discrimination between low, intermediate and high-grade stenotic coronary plaques is of importance. In recent years, a large number of studies have evaluated the performance of quantitative MDCT approaches to assess the degree of coronary stenosis in a direct comparison to invasive imaging techniques, including invasive coronary angiography and grey-scale intravascular ultrasound (IVUS).[5-10] An interesting study was performed by Leber et al[6] who evaluated the accuracy of a manual quantification approach for assessment of the degree of lumen diameter stenosis as compared to invasive angiographic evaluation with quantitative coronary angiography (QCA) and grey-scale IVUS. Using MDCT images, the grade of stenosis was determined by dividing the minimal lumen diameter at the level of the stenosis through the lumen diameter at the adjacent non-diseased region. Quantitative measurements were performed in longitudinal multiplanar curved reconstructions in two projections similar as those used for QCA. In total, MDCT and invasive coronary angiography were performed in 55 consecutive patients with known or suspected coronary atherosclerosis, of whom 18 patients underwent a combined examination with grey-scale IVUS. Reliable quantitative analysis could be performed in 825 coronary segments (using the 15-segment model). Overall, MDCT showed an only moderate correlation with QCA (r=0.54) and IVUS (r=0.61) for quantification of the degree of coronary stenosis. Importantly, sub-analysis showed that quantification was particularly challenging in distal coronary tree segments (segment 8 and 13) and marginal coronary branches (segment 12, 14 and 15). Additionally, coronary segments with heavily calcified lesions showed more often misclassifications when compared to coronary segments without severe calcified lesions. Moreover, it is important to note that the degree of luminal obstruction was significantly underestimated with MDCT as compared to grey-scale IVUS (41.1%±22.7% vs. 50.4%±14.0%, p<0.01). More recently, Cheng et al[11] sought to determine the relation between a visual multi-tiered grading system, semi-automated MDCT quantification of stenosis severity and QCA in 84 patients who had undergone invasive coronary angiography and MDCT imaging. Only interpretable native coronary segments with a diameter stenosis of ≥25% were included. All non-stented coronary segments were evaluated by two experienced and blinded MDCT readers who visually graded segments as follows: 0=0%, 1=1 - 24%, 2=25 - 49%, 3=50 - 69%, 4=70 - 89%, 5=90 - 100%. All coronary segments were also quantified by a semi-automated approach using a manually determined proximal and distal reference region, representing an approximation of the normal coronary vessel tapering. The reference regions were used to determine luminal narrowing at the level of maximal diameter stenosis (lesion marker) on longitudinal images. Consecutively, the degree of coronary stenosis, as derived from visual and semi-automated MDCT analysis, was compared to QCA. In total, 278 coronary segments with ≥25% diameter stenosis were included. Overall, the multi-tiered visual scoring system showed good correlation to QCA (Kendall's tau-b 0.76, weighted kappa 0.70, p<0.05). Of note, the semi-automated MDCT approach showed no improvement in diagnostic accuracy when compared to expert visual grading. One of the potential explanations for these findings may be the fact that the use of semi-automated quantification was associated with large variability introduced by manual interference. The minimal luminal diameter, the proximal and distal reference points were assessed manually, as indicated in Figure 1, whereas

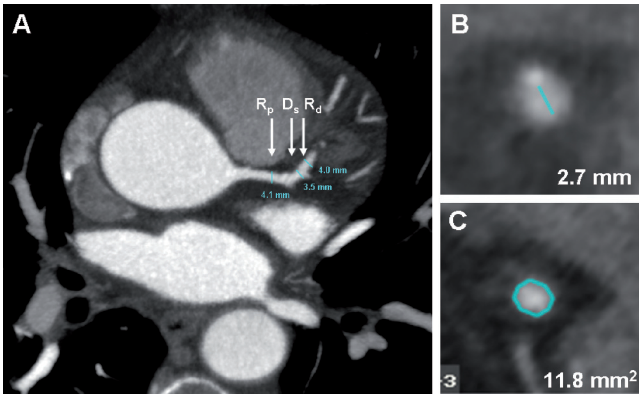


*Figure 1. Quantification of stenosis severity on multidetector row computed tomography (MDCT). Diameter coronary stenosis can be manually determined by assessing the lumen diameter at the lesion site and proximal/distal reference sites using either axial slices (panel A) or cross-sectional images perpendicular to the centreline of the vessel (panel B). Similarly, area stenosis can be calculated by tracing lumen areas on the cross-sectional images (panel C).*

a computed-assisted approach could have improved the accuracy of the quantitative measurements.

Recently, Joshi et al[10] aimed to determine the performance of quantitative computer-assisted MDCT analysis in 48 patients using grey-scale IVUS as the standard of reference. Quantitative coronary angiographic MDCT analysis was used to calculate percentage diameter stenosis on cross-sectional images. At first, semi-automated detection of coronary lumen centreline was performed with the use of vessel callipers, which could be manually adapted to ensure true coronary lumen detection. Consecutively, proximal and distal reference regions were defined by hand, after which the program automatically calculated minimal lumen diameter and minimal lumen area as well as the degree of percentage diameter stenosis. In this study, a moderate correlation between MDCT and IVUS was found for minimal lumen area ($r2=0.41$, $p<0.01$), whereas no correlation was found between MDCT and QCA for minimal lumen diameter ($r2=0.01$, $p=0.57$) or diameter stenosis ($r2=0.02$, $p=0.31$). For moderate to severe calcified lesions, MDCT showed no correlation for minimal lumen diameter ($r2<0.01$) and area ($r2<0.01$) as well as percentage diameter stenosis ($r2=0.06$) as compared to IVUS. However, for mildly calcified or non-calcified lesions, MDCT showed significantly improved correlations with IVUS for minimal lumen diameter ($r2=0.40$) and minimal lumen area ($r2=0.68$).

Currently, the majority of studies have used semi-manual MDCT approaches rather than dedicated automated segmentation algorithms to quantify stenosis severity. Recently, the feasibility of a novel dedicated algorithm for automated quantification of the degree of coronary stenosis was shown in a subset of 93 patients with known and suspected CAD.[12] In this study, performance of the novel quantitative algorithm was evaluated against QCA measurements in 282 coronary lesions. Quantitative analysis involved several automated processing steps, with less manual interference when compared to previous attempts to calculate the degree of stenosis (Figure 2). A 3D centreline of the region of interest (ranging from proximal to distal marker) was obtained with the use of a fast vessel tracking algorithm, which consisted of: (1) pre-segmentation of the coronary vessel and (2) fastest path back-tracking from distal to the proximal point. The 3D centreline was used to generate a multiplanar reconstructed volume and four longitudinal cross-sections of the region of interest. Finally, coronary lumen borders were detected by a model guided minimum cost approach (MCA) and used to quantify the percentage diameter stenosis. The MCA used spatial first-, and second-derivative gradient filters combined with knowledge of the expected intracoronary CT intensity to detect the contours. The study showed good correlations for quantification of percentage diameter stenosis on a vessel- ($n=282$, $r=0.83$, $p<0.01$) and patient basis ($n=93$, $r=0.86$, $p<0.01$), as shown in Figure 3. Importantly, MDCT scans were also visually scored using a binary scoring system with 50%

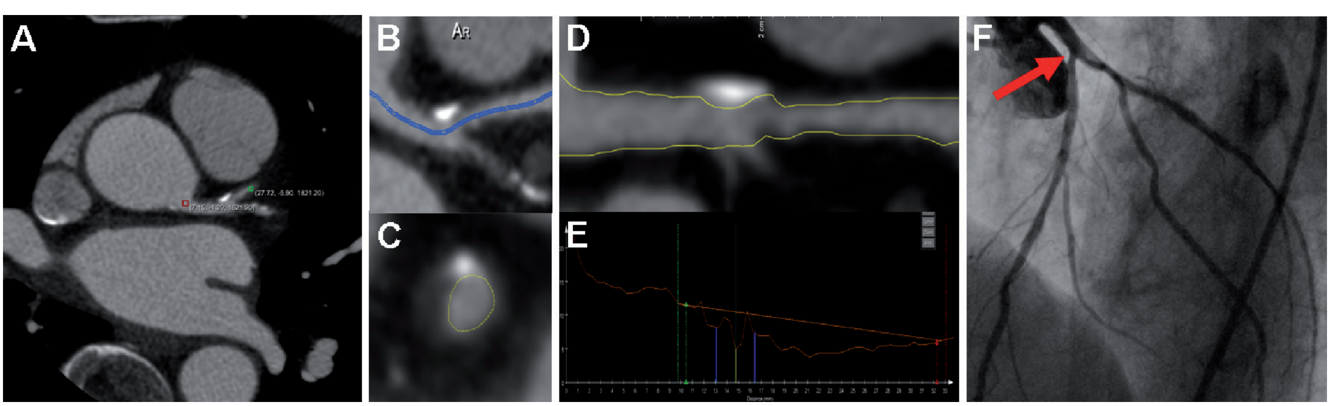


*Figure 2. Illustration of automated quantification of stenosis severity on multidetector row computed tomography (MDCT). The automated process involved several consecutive processing steps: (A) Determination of proximal (red) and distal (green) reference markers on axial slices; (B) Automated generation of the lumen centreline ranging from the proximal to distal reference marker; (C) Automated detection of lumen contours in transversal and (D) longitudinal planes; (E) Quantification of stenosis severity was based on the interrelation between lumen diameter at the site of minimal lumen diameter (yellow line, panel E) and the corresponding reference diameter (oblique orange line, panel E). The reference line in panel E was generated from proximal (green markers) and distal reference (red markers) regions. For this lesion (indicated by the blue markers, panel E), the maximal degree of stenosis was 39.0%. Corresponding invasive coronary angiography view was shown in panel F. Data based on reference 12.*

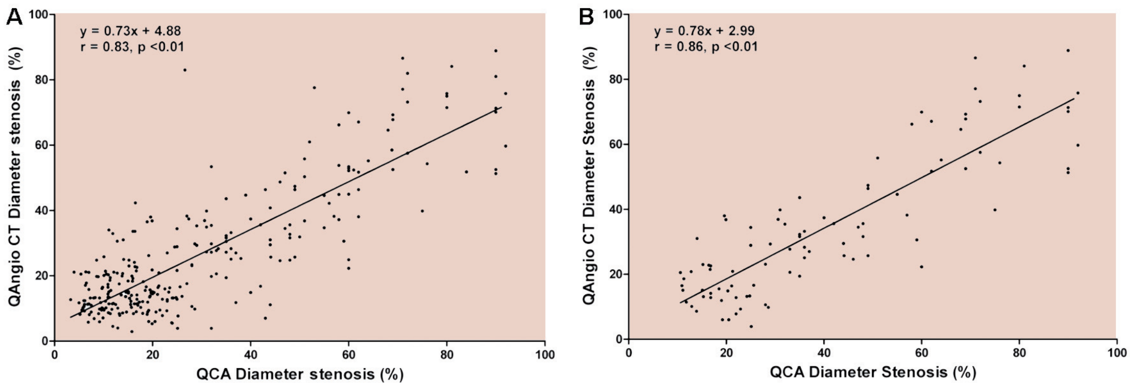


*Figure 3. Automated quantification of diameter stenosis (%) using dedicated software (QAngioCT) showed good correlation with quantitative coronary angiography (QCA) on a vessel basis (panel A) (n=282, r=0.83, p<0.01) and patient-basis (panel B) (n=93, r=0.86, p<0.01). Data based on reference 12.*

diameter stenosis as a cut-off. An improved diagnostic accuracy (95% vs. 87%, p=0.08) and positive predictive value (100% vs. 78%, p<0.05) was found for assessment of significant lesions (≥50% diameter stenosis) using quantitative MDCT analysis as compared to visual analysis.

Despite these promising results, one has to take into consideration that the use of quantitative MDCT algorithms is currently only feasible in data sets with good or moderate image quality. In case of severe cardiac motion artefacts, decreased image/noise ratio or suboptimal contrast arrival, the consistency of quantitative analyses may be distorted, and if so, visual interpretation may be preferred in these data sets. Additionally, quantification of atherosclerotic lesions located at coronary bifurcations remains challenging. In such lesions, visual analysis to evaluate stenosis severity may be preferred, rather than automated quantitative MDCT analysis. However, further improvement in quantitative MDCT algorithms may enhance the diagnostic accuracy of automated quantification and extend the analysis to more difficult cases. Moreover, rapid technological developments have led to considerable improvement in spatial and temporal resolution of the currently available MDCT scanners. Potentially, the introduction of new MDCT scanners as well as the continuous refinement of acquisition and post-processing protocols may even further improve diagnostic image quality of MDCT coronary angiography, resulting in an increased number of data sets suitable for automated MDCT quantification.

## Quantitative analysis of coronary plaque characteristics

MDCT enables a comprehensive non-invasive evaluation of coronary atherosclerosis beyond the isolated detection of significant coronary artery stenosis. It provides information on location, extent and distribution of coronary atherosclerotic plaques as well as a wide variety of additional geometric plaque characteristics, including plaque volume, plaque length and the degree of remodelling (Figure 4). These variables may be valuable for risk stratification as well as for planning of therapeutic coronary interventions.[13,14]

Currently, comprehensive evaluation of the presence and extent of coronary atherosclerosis is usually performed by visual analysis of MDCT images. However, one of the major limitations of visual MDCT analysis of plaque characteristics remains the fact that it is observer dependent and requires substantial experience. Accordingly, several attempts have been made that sought to determine the performance of automated or computed-based algorithms for quantification of plaque characteristics without extensive manual interference. The use of automated quantitative algorithms may potentially improve the robustness and reproducibility of MDCT analyses, and importantly, the combined post-processing and interpretation of MDCT data sets may become less time-consuming. Moreover, quantification of plaque characteristics (e.g., plaque volume) with an automated and robust approach becomes of special interest when using MDCT to assess progression of coronary atherosclerosis.

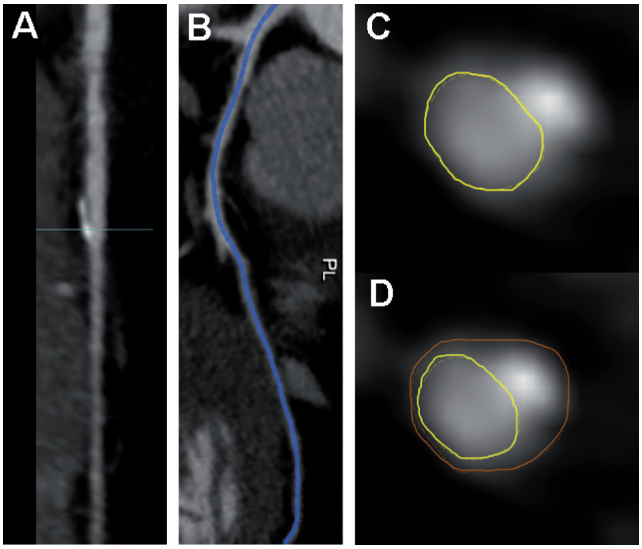


*Figure 4. Multidetector row computed tomography (MDCT) provides a comprehensive overview of the coronary anatomy and coronary atherosclerosis. The location, extent and morphology of atherosclerotic plaques can be derived using multiplanar reconstructed volumes (panel A and B). Additionally, with the use of quantitative algorithms, detection of lumen (panel C) and outer vessel wall (panel D) contours can be performed based on image gradients and lumen centre lines. Consecutively, the detected contours allow evaluation of stenosis severity, plaque burden, plaque length and the degree of remodelling.*

## Plaque morphology

In recent years, the non-invasive evaluation of plaque morphology and plaque configuration gained increasingly interest in clinical cardiology, as these variables may be important predictors for plaque rupture and acute coronary events.[13,15] For this reason, several studies have sought to evaluate the potential of MDCT to quantify coronary plaque composition.[16-18] Schroeder et al[16] evaluated the diagnostic accuracy of plaque composition analysis on MDCT using IVUS as the standard of reference. In total, 34 coronary plaques of 15 patients with chronic stable anginal complaints were identified on both imaging modalities, including non-calcified (n=12), mixed (n=5) and calcified (n=17) atherosclerotic lesions. Differentiation of plaque composition was performed visually by an expert observer. For each plaque type, the mean attenuation (expressed in Hounsfield units [HU]) of 16 randomly selected locations within the intracoronary plaque (defined as >40% luminal narrowing) was measured using a dedicated post-processing software. On MDCT, the mean attenuation was 14±26 HU for non-calcified lesions, whereas mixed and calcified lesions showed a mean attenuation of 91±21 HU and 419±194 HU, respectively. Moreover, the mean attenuation values on MDCT were significantly different for each IVUS-derived plaque type ($p<0.05$). More recently, Leber et al[18] performed a study that aimed to assess the accuracy of plaque type characterisation on MDCT in 46 patients with an increased risk profile. For each coronary plaque, density measurements (HU) were performed at each 3 mm coronary section using axial slices. After a raster consisting of 1 $mm^2$ boxes was placed for each 3 mm section, density measurements were performed on five randomly selected locations. In this study, the mean attenuation values were 49±22 HU (hypo-echoic), 91±22 HU (hyper-echoic) and 391±156 HU (calcified lesions). Accordingly, these studies have indicated that MDCT imaging can be used to quantify different types of plaque morphology. However, it has also been demonstrated that further classification of plaque type using MDCT can be difficult. Using IVUS, Pohle et al[19] demonstrated that mean MDCT density was significantly lower in lesions consisting mainly of fibrofatty tissue as compared to fibrotic lesions. Nevertheless, between individual lesions, substantial overlap in density values was noted. Similar findings were reported by Choi et al[20], evaluating 80 non-calcified plaques and compared findings to intravascular ultrasound radiofrequency analysis (VH-IVUS). In addition, differences in acquisition characteristics, including flow rate and contrast agent, as well as patient characteristics such as cardiac output and body weight, may substantially influence individual measurements. Finally, one should also be aware of the restrictions in spatial resolution of MDCT. In calcified lesions, the blooming effect of the calcium may result in overestimation of the extent of calcium and inaccurate classification of adjacent plaque areas. Vice versa, one has to take into consideration that plaques deemed to be entirely non-calcified on MDCT may contain small amounts of calcium.[21]

## Plaque volume, burden and remodelling index

A large number of studies have aimed to quantify plaque volume, burden and the degree of remodelling using semi-automated MDCT approaches.[7,9,13,22] Leber et al[7] sought to determine the accuracy of plaque volume measurements using MDCT as compared to invasive grey-scale IVUS in 20 patients. For both techniques, the total plaque volume was measured by adding the semi-automated detected plaque area per coronary section. The study showed a good correlation for plaque volume ($r2=0.69$, $p<0.01$) (Figure 5) between both imaging modalities, with a significant underestimation for mixed (47.7±87.5 $mm^3$ vs. 57.5±99.4 $mm^3$, $p<0.05$) and non-calcified (59.8±76.6 $mm^3$ vs. 67.7±67.9 $mm^3$, $p<0.05$) plaques. Calcified lesions were slightly overestimated on MDCT when compared to IVUS (65.8±110.0 $mm^3$ vs. 53.2±90.3 $mm^3$, $p=0.19$). In addition, Bruining and colleagues[9] used an automated MDCT approach with limited manual interference to assess plaque volume using IVUS as the standard of reference. In 48 symptomatic patients, computed-assisted coronary plaque MDCT measurements were performed by two independent observers. After the regions of interest were matched for both techniques, they were extracted from the 3D data set with the use of semi-automated vessel

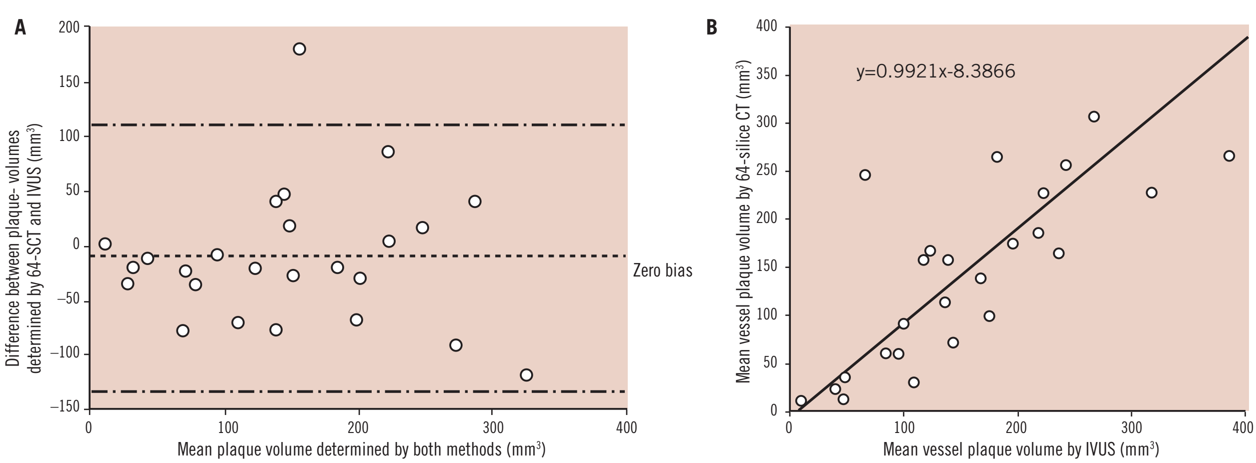


*Figure 5. Semi-automated quantification of plaque volume as assessed with multidetector row computed tomography (MDCT) and intravascular ultrasound (IVUS). A. Plaque volume was systematically underestimated with MDCT as compared to IVUS as shown in the Bland-Altman Analysis (p<0.05). B. Good correlation was found for quantification of plaque volume between both techniques (r2=0.69, p<0.01). Data based on reference 7.*

extraction software (CURAD). Thereafter, for each region of interest, lumen borders were automatically detected on the basis of an edge-detection method using a dedicated filter (digital Deriche filter) which calculated the gradient of the images. Of note, the automated edge-detection method could only be used for detection of lumen borders, whereas the vessel wall borders were manually outlined. Using this approach, plaque volume was significantly overestimated on MDCT when compared to IVUS (222±121 $mm^3$ vs. 189±93 $mm^3$, p<0.01). Importantly, for both readers, good correlations were found between MDCT and IVUS for plaque volume (r=0.74 and r=0.79). Similarly, Otsuka et al[22] evaluated the accuracy of quantitative plaque volume MDCT measurements in 47 patients as compared to IVUS. After coronary-tree extraction was performed, plaque volume and plaque burden were measured using manually-traced MDCT lumen and vessel wall contours (Figure 6). The study found good correlations for regional plaque burden (r=0.96, p<0.01) and plaque volume (r=0.98, p<0.01) between quantitative CT and IVUS. In addition, good reproducibility was observed as indicated by a Pearson's correlation coefficient of 0.98 (p<0.001) and 0.91 (p<0.001), respectively, for intra-observer and interobserver correlation.

Coronary plaque remodelling has also been recognised as an important plaque characteristic that has been linked to increased vulnerability.[13,15] With IVUS as the standard of reference, several studies have explored the potential of MDCT to assess coronary plaque remodelling.[13,23] Achenbach et al[23] evaluated the feasibility of MDCT to evaluate remodelling index in 44 patients with known atherosclerotic plaques. In this study, plaque remodelling was calculated by dividing the manually-traced cross-sectional vessel wall area at the level of maximal luminal narrowing by the cross-sectional vessel wall area at the proximal non-diseased reference region, as indicated in Figure 7. Interestingly, the study demonstrated

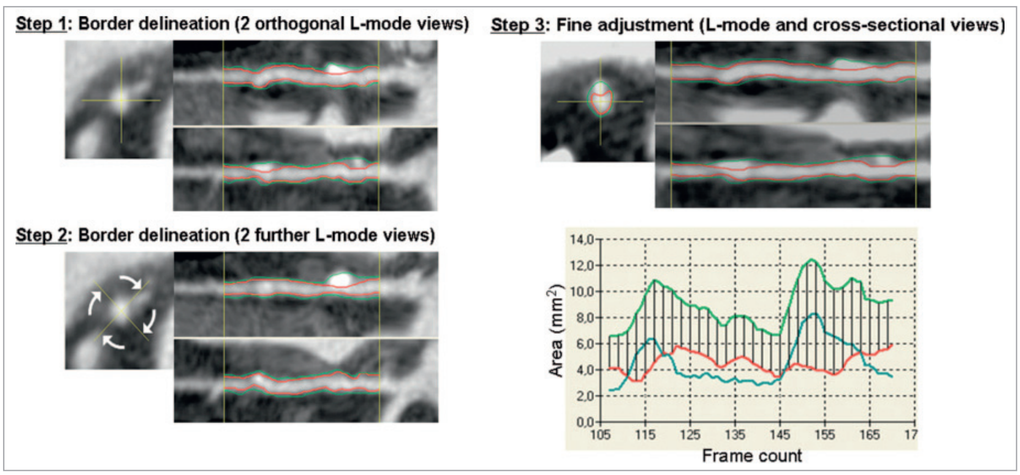


*Figure 6. Schematic illustration of plaque burden quantification as assessed with multidetector row computed tomography (MDCT). Coronary arteries were extracted using semi-automated vessel extraction software. For each coronary artery, lumen plaque interface (red lines) and the outer vessel wall border (green lines) were identified and manually delineated in at least 4 orthogonal L-mode views with rotational display of the extracted coronary artery (step 1 and 2). Further refinement of the contour tracing was performed by referring to the corresponding transversal images (step 3). Finally, plaque burden (blue line) was derived from the interrelation of vessel wall area (green line) and lumen area (red line). Reprinted with permission from reference 22.*

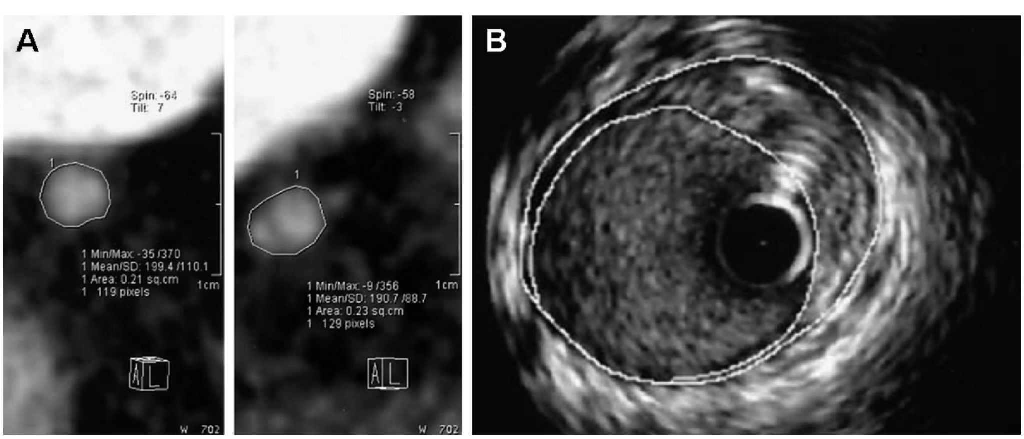


*Figure 7. Quantitative approach for assessment of coronary plaque remodelling using multidetector row computed tomography (MDCT) (panel A) and IVUS (panel B). With MDCT, remodelling index was calculated using manually-traced outer vessel wall area at the site of maximal luminal narrowing (right panel) and non-diseased proximal reference region (left panel). A similar approach was used to calculate the degree of plaque remodelling on IVUS. For both imaging modalities, the degree of remodelling was calculated by dividing the vessel wall area at the level of the maximal stenosis by the proximal reference vessel wall area. Reprinted with permission from reference 23.*

that the degree of remodelling was significantly higher in patients with non-stenotic lesions as compared to patients with stenotic lesions (1.3±0.2 vs. 1.0±0.2, p<0.01). Moreover, remodelling index as derived from MDCT showed good correlation with IVUS (r2=0.82, p<0.01).

## Future challenges

A systematic evaluation of atherosclerotic lesions requires the detection of both lumen and outer vessel wall borders throughout the coronary tree. Although the feasibility for automated detection of luminal borders has been demonstrated[12], the automated detection of outer vessel wall borders remains a challenge as it is usually hampered by subtle differences in image gradients, particularly in peripheral coronary segments. A fully automated approach for detection of outer vessel wall borders has not been validated yet for clinical practice. Accordingly, the feasibility to quantify plaque volume, burden and remodelling index have only been demonstrated using semi-automated vessel wall border detection.[7,9,13,22] With the currently applied algorithms, extensive manual interference is still required to generate reliable outer vessel wall borders. Potentially, the introduction of advanced quantitative algorithms (which are currently in development) in combination with advances in scanner technology may further improve the consistency of vessel wall and reference contour detection, leading to improved quantification of plaque characteristics.

## Quantitative computed tomography angiography to guide percutaneous coronary interventions

Non-invasive evaluation of coronary atherosclerosis with the use of MDCT imaging provides important information which can be used to guide percutaneous coronary interventions. MDCT provides integrated information on extent, location and distribution of coronary atherosclerosis, beyond the isolated assessment of coronary stenosis severity. More in-depth pre-procedural evaluation of coronary plaques (stenosis severity, plaque location and length) may be valuable for procedural planning and may increase procedural success. For example, it has been recently demonstrated that depicting the degree of calcification and the length of an occluded segment on MDCT (which can be difficult on invasive coronary angiography but can be easily derived from MDCT) may predict the success of percutaneous treatment of chronic total coronary artery occlusions.[24] Bifurcation lesions represent another challenge in interventional cardiology. One of the underlying mechanisms of the observed lower angiographic success rate of these lesions is the occurrence of coronary plaque shifting or rupture, which may lead an occlusion of coronary side branches. Pre-interventional MDCT assessment of the coronary angulation and tortuosity as well as plaque location, severity and composition could potentially prevent difficult and high-risk percutaneous procedures.

## Conclusions

MDCT imaging provides a comprehensive evaluation of coronary anatomy and atherosclerosis. The majority of studies have used semi-automated algorithms to quantify a wide variety of plaque characteristics, predominantly focusing on the degree of luminal narrowing. Despite promising findings, further refinement of the quantitative MDCT algorithms is currently indicated. With the introduction of such improved quantitative post-processing algorithms, however, fully automated analysis of plaque characteristics may become feasible and may provide valuable information for the diagnosis and management of patients with CAD.

## References


1. Hoffmann MH, Shi H, Schmitz BL, Schmid FT, Lieberknecht M, Schulze R, Ludwig B, Kroschel U, Jahnke N, Haerer W, Brambs HJ, Aschoff AJ. Noninvasive coronary angiography with multislice computed tomography. *JAMA* 2005;293:2471-2478.

2. Miller JM, Rochitte CE, Dewey M, rbab-Zadeh A, Niinuma H, Gottlieb I, Paul N, Clouse ME, Shapiro EP, Hoe J, Lardo AC, Bush DE, de RA, Cox C, Brinker J, Lima JA. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008;359:2324-2336.

3. Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, Nieman K, van Werkhoven JM, Pundziute G, Weustink AC, de Vos AM, Pugliese F, Rensing B, Jukema JW, Bax JJ, Prokop M, Doevendans PA, Hunink MG, Krestin GP, de Feyter PJ. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J Am Coll Cardiol* 2008;52:2135-2144.

4. Scanlon PJ, Faxon DP, Audet AM, Carabello B, Dehmer GJ, Eagle KA, Legako RD, Leon DF, Murray JA, Nissen SE, Pepine CJ, Watson RM, Ritchie JL, Gibbons RJ, Cheitlin MD, Gardner TJ, Garson A, Jr., Russell RO, Jr., Ryan TJ, Smith SC, Jr. ACC/AHA guidelines for coronary angiography. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Coronary Angiography). Developed in collaboration with the Society for Cardiac Angiography and Interventions. *J Am Coll Cardiol* 1999;33:1756-1824.

5. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. *J Am Coll Cardiol* 2005;46:552-557.

6. Leber AW, Knez A, von ZF, Becker A, Nikolaou K, Paul S, Wintersperger B, Reiser M, Becker CR, Steinbeck G, Boekstegers P. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005;46:147-154.

7. Leber AW, Becker A, Knez A, von ZF, Sirol M, Nikolaou K, Ohnesorge B, Fayad ZA, Becker CR, Reiser M, Steinbeck G, Boekstegers P. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. *J Am Coll Cardiol* 2006;47:672-677.

8. Husmann L, Gaemperli O, Schepis T, Scheffel H, Valenta I, Hoefflinghaus T, Stolzmann P, Desbiolles L, Herzog BA, Leschka S, Marincek B, Alkadhi H, Kaufmann PA. Accuracy of quantitative coronary angiography with computed tomography and its dependency on plaque composition: plaque composition and accuracy of cardiac CT. *Int J Cardiovasc Imaging* 2008;24:895-904.

9. Bruining N, Roelandt JR, Palumbo A, La GL, Cademartiri F, de Feijter PJ, Mollet N, van Domburg RT, Serruys PW, Hamers R. Reproducible coronary plaque quantification by multislice computed tomography. *Catheter Cardiovasc Interv* 2007;69:857-865.

10. Joshi SB, Okabe T, Roswell RO, Weissman G, Lopez CF, Lindsay J, Pichard AD, Weissman NJ, Waksman R, Weigold WG. Accuracy of com-

puted tomographic angiography for stenosis quantification using quantitative coronary angiography or intravascular ultrasound as the gold standard. *Am J Cardiol* 2009;104:1047-1051.

11. Cheng V, Gutstein A, Wolak A, Suzuki Y, Dey D, Gransar H, Thomson LE, Hayes SW, Friedman JD, Berman DS. Moving beyond binary grading of coronary arterial stenoses on coronary computed tomographic angiography: insights for the imager and referring clinician. *JACC Cardiovasc Imaging* 2008;1:460-471.

12. Boogers MJ, Schuijf JD, Kitslaar PH, van Werkhoven JM, de Graaf FR, Boersma E, van Velzen JE, Dijkstra J, Adame IM, Kroft LJ, de Roos A, Schreur JHM, Heijenbrok MW, Jukema JW, Reiber JHC, Bax JJ. Novel Dedicated Approach for Automated Quantification of Stenosis Severity on 64-Slice Multi-slice Computed Tomography: A Comparison with Quantitative Coronary Angiography. *JACC Cardiovasc Imaging* 2010. In press.

13. Motoyama S, Kondo T, Sarai M, Sugiura A, Harigaya H, Sato T, Inoue K, Okumura M, Ishii J, Anno H, Virmani R, Ozaki Y, Hishida H, Narula J. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. *J Am Coll Cardiol* 2007;50:319-326.

14. Bluemke DA, Achenbach S, Budoff M, Gerber TC, Gersh B, Hillis LD, Hundley WG, Manning WJ, Printz BF, Stuber M, Woodard PK. Noninvasive coronary artery imaging: magnetic resonance angiography and multidetector computed tomography angiography: a scientific statement from the american heart association committee on cardiovascular imaging and intervention of the council on cardiovascular radiology and intervention, and the councils on clinical cardiology and cardiovascular disease in the young. *Circulation* 2008;118:586-606.

15. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. *J Am Coll Cardiol* 2006;47(8 Suppl):C13-C18.

16. Schroeder S, Kopp AF, Baumbach A, Meisner C, Kuettner A, Georg C, Ohnesorge B, Herdeg C, Claussen CD, Karsch KR. Noninvasive detection and evaluation of atherosclerotic coronary plaques with multislice computed tomography. *J Am Coll Cardiol* 2001;37:1430-1435.

17. Hur J, Kim YJ, Lee HJ, Nam JE, Choe KO, Seo JS, Choi DH, Kim JS, Choi BW. Quantification and characterization of obstructive coronary plaques using 64-slice computed tomography: a comparison with intravascular ultrasound. *J Comput Assist Tomogr* 2009;33:186-192.

18. Leber AW, Knez A, Becker A, Becker C, von ZF, Nikolaou K, Rist C, Reiser M, White C, Steinbeck G, Boekstegers P. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: a comparative study with intracoronary ultrasound. *J Am Coll Cardiol* 2004;43:1241-1247.

19. Pohle K, Achenbach S, MacNeill B, Ropers D, Ferencik M, Moselewski F, Hoffmann U, Brady TJ, Jang IK, Daniel WG. Characterization of non-calcified coronary atherosclerotic plaque by multidetector row CT: comparison to IVUS. *Atherosclerosis* 2007;190:174-180.

20. Choi BJ, Kang DK, Tahk SJ, Choi SY, Yoon MH, Lim HS, Kang SJ, Yang HM, Park JS, Zheng M, Hwang GS, Shin JH. Comparison of 64-slice multidetector computed tomography with spectral analysis of intravascular ultrasound backscatter signals for characterizations of noncalcified coronary arterial plaques. *Am J Cardiol* 2008;102:988-993.

21. Pundziute G, Schuijf JD, Jukema JW, Decramer I, Sarno G, Vanhoenacker PK, Reiber JH, Schalij MJ, Wijns W, Bax JJ. Head-to-head comparison of coronary plaque evaluation between multislice computed tomography and intravascular ultrasound radiofrequency data analysis. *JACC Cardiovasc Interv* 2008;1:176-182.

22. Otsuka M, Bruining N, Van Pelt NC, Mollet NR, Ligthart JM, Vourvouri E, Hamers R, De JP, Wijns W, van Domburg RT, Stone GW, Veldhof S, Verheye S, Dudek D, Serruys PW, Krestin GP, de Feyter PJ. Quantification of coronary plaque by 64-slice computed tomography: a comparison with quantitative intracoronary ultrasound. *Invest Radiol* 2008;43:314-321.

23. Achenbach S, Ropers D, Hoffmann U, MacNeill B, Baum U, Pohle K, Brady TJ, Pomerantsev E, Ludwig J, Flachskampf FA, Wicky S, Jang IK, Daniel WG. Assessment of coronary remodeling in stenotic and nonstenotic coronary atherosclerotic lesions by multidetector spiral computed tomography. *J Am Coll Cardiol* 2004;43:842-847.

24. Garcia-Garcia HM, van Mieghem CA, Gonzalo N, Meijboom WB, Weustink AC, Onuma Y, Mollet NR, Schultz CJ, Meliga E, van der EM, Sianos G, Goedhart D, den Boer A, de Feyter P, Serruys PW. Computed tomography in total coronary occlusions (CTTO registry): radiation exposure and predictors of successful percutaneous intervention. *EuroIntervention* 2009;4:607-616.